

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6: <b>G01N 23/20</b>		A1	(11) International Publication Number: <b>WO 96/38722</b>
			(43) International Publication Date: 5 December 1996 (05.12.96)
(21) International Application Number: <b>PCT/US96/07555</b>		(81) Designated States: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT, UA, UG, UZ, VN, ARIPO patent (KR, LS, MW, SD, SZ, UG), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 31 May 1996 (31.05.96)			
(30) Priority Data: 454,909 31 May 1995 (31.05.95) US			
(71) Applicants: QUANTA VISION, INC. [US/US]; Suite #214, 1670 S. Amphlett Boulevard, San Mateo, CA 94402 (US).			
(72) Inventors: KURBATOV, Alexey V.; Apartment 18, Izumrudnaya 11, Moscow, 129281 (RU). LAZAREV, Pavel, I.; 806 Coleman Avenue #21, Menlo Park, CA 94025 (US).		Published With international search report. With amended claims and statement.	
(74) Agents: MILLERS, David, T. et al.; Skjerven, Merrill, MacPherson, Franklin & Friel, Suite 700, 25 Metro Drive, San Jose, CA 95110 (US).			
(54) Title: X-RAY AND NEUTRON DIFFRACTOMETRIC IMAGING OF THE INTERNAL STRUCTURE OF OBJECTS			
(57) Abstract			
<p>A method and device for examining the internal structure of an object uses diffracted x-rays or other penetrating radiation. In one embodiment spatial filters (120, 130) proximate to a source of radiation (110) transmit an array of divergent pixel-beams (133), which irradiate an object (140) being examined. The object absorbs, refracts, diffracts and incoherently scatters radiation from the pixel-beams. Spatial filters (150, 160) proximate to a detector (170) block undeflected and unrefracted radiation which exits the object. The detector separately measures diffracted radiation from each pixel-beam.</p>			

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AM	Armenia	GB	United Kingdom	MW	Malawi
AT	Austria	GE	Georgia	MX	Mexico
AU	Australia	GN	Guinea	NE	Niger
BB	Barbados	GR	Greece	NL	Netherlands
BE	Belgium	HU	Hungary	NO	Norway
BF	Burkina Faso	IE	Ireland	NZ	New Zealand
BG	Bulgaria	IT	Italy	PL	Poland
BJ	Benin	JP	Japan	PT	Portugal
BR	Brazil	KE	Kenya	RO	Romania
BY	Belarus	KG	Kyrgyzstan	RU	Russian Federation
CA	Canada	KP	Democratic People's Republic of Korea	SD	Sudan
CF	Central African Republic	KR	Republic of Korea	SE	Sweden
CG	Congo	KZ	Kazakhstan	SG	Singapore
CH	Switzerland	LI	Liechtenstein	SI	Slovenia
CI	Côte d'Ivoire	LK	Sri Lanka	SK	Slovakia
CM	Cameroon	LR	Liberia	SN	Senegal
CN	China	LT	Lithuania	SZ	Swaziland
CS	Czechoslovakia	LU	Luxembourg	TD	Chad
CZ	Czech Republic	LV	Latvia	TE	Togo
DE	Germany	MC	Monaco	TJ	Tajikistan
DK	Denmark	MD	Republic of Moldova	TT	Trinidad and Tobago
EE	Estonia	MG	Madagascar	UA	Ukraine
ES	Spain	ML	Mali	UG	Uganda
FI	Finland	MN	Mongolia	US	United States of America
FR	France	MR	Mauritania	UZ	Uzbekistan
GA	Gabon			VN	Viet Nam

WO 96/38722

PCT/US96/07555

X-RAY AND NEUTRON DIFFRACTOMETRIC IMAGING  
OF THE INTERNAL STRUCTURE OF OBJECTS

BACKGROUND OF THE INVENTION5 Field of the Invention

The present invention relates to using diffraction of penetrating radiation to image or analyze the internal structure of objects such as biological objects, plastics, metals, and other materials with  
10 ordered molecular or atomic structures.

Description of Related Art

When a beam of penetrating radiation such as X-rays or neutrons is incident on an object, the beam  
15 is affected by absorption and scattering. Conventional X-ray radiography forms images showing a pattern of absorption of X-rays in an object. In conventional radiography, scattering is a parasitic effect. Scattering has several distinct mechanisms such as non-  
20 coherent scattering, refraction, and diffraction. Recently, Mitrofanov (British patent publication 2317453), Belyaevskaya (PCT International publication WO 92/21016) and Wilkins (PCT International publication WO 95/05725) proposed approaches for refractive imaging  
25 of the objects.

The refractometric imaging systems of Mitrofanov and Belyaevskaya use detectors which rely on Bragg diffraction in crystals to detect refracted radiation. These systems require an initial beam with a high  
30 spectral purity (i.e. monochromatic radiation or radiation in a narrow spectral band) and a high spatial coherence (i.e. parallel radiation or radiation with a small angular divergence). Wilkins proposed a system which reduces the requirement for spectral purity by  
35 using an angle analyzer that does not rely on Bragg diffraction. Wilkins' system can use radiation with a wider wavelength band (a wider spectral range) because

WO 96/38722

PCT/US96/07555

refraction does not strongly depend upon wavelength and the detector does not use Bragg diffraction which would introduce wavelength dependence.

The systems of Mitrofanov, Belyaevskaya, and Wilkins all detect radiation refracted in objects. Measuring the small angular deviations caused by refraction of penetrating radiation requires high spatial coherence of initial radiation and extremely accurate measuring devices. Narrow collimation of radiation from a source can provide a beam with high spatial coherence, but such narrow collimation uses only a small portion of the radiation from a typical source. Typically, only  $10^3$  to  $10^4$  of the total photon flux emitted by the source is usable. Accordingly, imaging a large object using a refractive system may require too much energy to be practical.

Imaging systems are needed that are more energy efficient and capable of quickly forming images of large objects.

#### SUMMARY OF THE INVENTION

Embodiments of the invention provide diffractometric imaging using radiation diffracted from objects containing chemical materials such as plastics, explosives, and crystals and biological materials such as muscle, mucus, cartilage, bones, hair, and feathers which have ordered atomic or molecular structures. One embodiment of the invention provides a method of imaging objects and performing an analysis of the structure and materials in objects. The method includes irradiating an object with a set of separate, divergent pixel-beams of penetrating radiation and detecting integrals of the intensity of diffracted radiation around each pixel-beam after the pixel-beam passes through the object.

WO 96/38722

PCT/US96/07555

Passing penetrating radiation through an array of apertures formed in a material that is non-transparent to the radiation forms pixel-beams. The separation between the apertures and therefore the initial separation between the pixel-beams should be large enough for a detector to resolve the distributions of intensity around each beam without interference from the diffracted intensity distributions of the neighboring pixel-beams. Allowing the pixel-beams to diverge from each other improves the detector's ability to resolve separate diffraction patterns and allows a greater portion of the flux from a radiation source to be used in imaging and analysis. For example, a hemishperical portion of the radiation flux can be divided into a set of pixel-beams that diverge by as much as 90° from the center of the radiation pattern.

For biological objects, typical apertures have diameter in a range from 20 to 100 microns and preferably within a range of from 20 to 60 microns. In order to increase sensitivity of the method, the radiation not deflected in the object and the refracted radiation which is deflected at small angles, in the range from 0 to 10 seconds of arc, are prevented from reaching the detector and hence are not detected. A filter, which includes an array of opaque regions placed in the path of the initial pixel-beams at a position between the object and the detector, can block the non-diffracted radiation. The size of the each opaque region corresponds to the size of a pixel-beam at the plane of the region plus a lateral extension to block radiation refracted from the pixel-beam.

An image of the object is formed from an array of pixels, each of which has an intensity determined from the intensity of diffracted radiation which is detected in the vicinity of a corresponding pixel-beam. The method also allows structural analysis of an object by

WO 96/38722

PCT/US96/07555

detecting radiation distributions in diffraction patterns around the pixel-beams. The radiation distributions around a pixel-beam contains information about ordered materials along the path of the pixel-beam through the object.

5 The angular positions of reflexes and their corresponded intensity provides information about the structure of the material which produced the diffraction pattern. The diffraction pattern can be used for medical diagnostic purposes such as distinguishing normal tissues from abnormal tissues (such as cancer) in biological objects or in security applications for identifying particular chemical compounds (such as explosives or contraband) in luggage or other sealed containers.

10 As an alternative to forming pixel-beams, passing penetrating radiation through a spatial filter containing an array of opaque regions or barriers forms an incident radiation pattern having an array of shadowed regions. For example, if a first spatial filter contains an array of apertures which forms an array pixel beams. An alternative spatial filter, which is opaque (transparent) where the first spatial filter is transparent (opaque), forms a radiation pattern that is the "negative" of the pattern of radiation in the pixel-beams. Diffraction in an object deflects some radiation into the shadowed regions, and the pattern of diffracted radiation in each shadowed region can be analyzed in the same manner as the diffraction pattern around a pixel-beam described above.

25 One embodiment of the invention is an apparatus for imaging and/or structural analysis of objects. The apparatus includes: a source of penetrating radiation; an object holder; and a first spatial filter placed between the source and the object holder. The first

WO 96/38722

PCT/US96/07558

spatial filter forms a spatially modulated pattern of penetrating radiation from the source. The spatially modulated pattern can contain divergent radiation from the source to increase efficiency. Use of  
5 divergent radiation improves efficiency because the divergence angle determines the fraction of the total flux which is spatially modulated to form the incident radiation pattern. To improve collimation and spatial coherence of the spatially modulated pattern, a second  
10 spatial filter can be placed between first spatial filter and the object holder. The second spatial filter contains a pattern of opaque regions which is the same as a pattern in the first spatial filter but is expanded in size according to distance from the  
15 source. A third spatial filter between the object holder and a detector has opaque regions along the non-deflected path of radiation from the first spatial filter to block non-deflected radiation and provide a dark field imaging system.

20

#### BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is a diagram of an imaging apparatus in accordance with an embodiment of the invention.

Fig. 2 illustrates the collimating part of an  
25 apparatus of Fig. 1.

Fig. 3 shows scattering of radiation in an object and an embodiment of spatial filters which discriminate an angular range of diffracted radiation for imaging or analysis.

30 Fig. 4 shows another embodiment of the spatial filters which select radiation for imaging or analysis.

Use of the same reference symbols in different figures indicates similar or identical items.

#### 35 DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

WO 96/38722

PCT/US96/07555

Diffraction of radiation occurs when particles such as atoms, molecules, sub-molecular fragments in an object have structure with some degree of order on a scale about equal to the wavelength of the radiation.

5 A perfect crystal is an example of a highly ordered structure. Gases have much less order. However even in a gas, molecules scatter radiation with a non-monotonic angular distribution about the direction an initial beam, and the distribution is characteristic of  
10 the molecules and supra-molecular clusters in the gas. Accordingly, the angular distribution of radiation scattered from a gas contains information about the structure of molecules in the gas and clusters which are formed by the molecules in the gas.

15 Diffracted radiation distributions are centrosymmetrical, and have characteristic patterns which can identify a material. Crystalline materials and many non-crystalline materials such as cellulose, mucus, muscle, cartilage, some plastics have ordered structure  
20 and distinct diffraction patterns. Other materials have diffusive diffraction patterns which still distinguish the degree of order in the structure. Distributions for some materials such as mucus and powdered monocrystals have circular maximums of  
25 intensity (or reflexes in the sense in which the term is used in the book "X-ray diffraction" by B. E. Warren, Dover Publication, Inc, NY). Mucus has circular reflexes because the orientation of molecules in mucus is relatively random. Material like muscle  
30 which contains fibers oriented in one direction have meridional and equatorial reflexes. Highly ordered materials such as monocrystalline materials have spotlike reflexes in a symmetrical pattern.

The angular distribution, symmetry, and intensity  
35 of the diffraction pattern from a material indicates the structure of the material. If a material contains



WO 96/38722

PCT/US96/07555

no prefer axis of orientation, a diffraction pattern is generally symmetric about a central axis of an initial beam and tends to contain separate circular reflexes.

If the material has a distinguishable axis of

- 5 orientation, the diffraction pattern tend to have axially variations and standalone reflexes of some form.

- The angles of diffraction of X-rays from an ordered structure are governed by Bragg's equation,  
10  $\sin(\theta) = n \cdot (\lambda) / (2 \cdot D)$ , where  $2\theta$  is the diffraction angle,  $n$  is an integer which is the order of diffraction maximum,  $\lambda$  is the X-ray wavelength, and  $D$  is period of ordered structure, i.e. the distance between repeating fragments. The periodicity  $D$  of  
15 structures has different values for different materials, and the composition of the periodic structure and the angle  $\theta$  determine the intensity of diffraction reflexes. For example, an intense reflex for mucus has periodicity  $D$  equal to 48 Å, and has  
20 angle  $\theta$  equal to 0.9° at wavelength  $\lambda$  of 0.71 Å. An intense reflex for one type of muscle is produced by periodic structure with periodicity  $D$  equal to 143 Å, which correspond to an angle  $\theta$  equal to 0.15°.

- For X-rays, diffraction angles are typically  
25 orders of magnitude larger than refraction angles. Typical refraction angles for X-rays in most materials are less than about 10 arcsec, and typical diffraction angles are two to three orders of magnitude larger. In the above examples, the diffraction angles are about  
30 540 arcsec for muscle and about 3000 arcsec for mucus. The large difference between scattering angles for diffraction and refraction means that equipment for measuring refracted radiation is often not suited for measuring diffracted radiation.

- 35 Fig. 1 shows an embodiment of an apparatus 100 for diffractive imaging and/or structural analysis of an

WO 96/38722

PCT/US96/07555

object 140. Object 140 can be any type of object to be imaged or analyzed. A holder adapted for the type of object 140 under investigation places and fixes object 140 for exposure to multiple pixel-beams 115 from a radiation source 110. The term pixel-beam as used herein indicates a beam used to obtain information about structure of a portion of object 140 along the path of the beam. In one embodiment, each pixel-beam is used to obtain information for one pixel in an image or projection of object 140. In medical applications, object 140 could be a patient or a sample, and conventional devices for placing patients and samples can be used. In security applications, conventional holders such as for holding luggage during scanning for weapons or explosives would be used.

Radiation source 110 is a conventional source of X-rays, neutrons, or other penetrating radiation. Examples of sources of such radiation include a Roentgen tube, a synchrotron, or radio active source such as a cobalt 60 gun. In one embodiment, source 110 is an X-ray tube with a filter-monochromator which provides nearly monochromatic radiation, with a diameter of focus (bright spot) of about 6 to 10 microns. In one embodiment, source 110 is a microfocus source. Such X-ray sources are well known standard devices in radiology.

A first spatial filter 120 and a second spatial filter 130 are between source 110 and object 140. Spatial filters 120 and 130 are constructed of a material that is opaque to the penetrating radiation from source 110, and each of spatial filter 120 and 130 contains an array of apertures 123 or 133. Each of the apertures 123 has a corresponding aperture 133 which is centered along a line from source 110 through corresponding apertures 123 and 133. Apertures 123 and 133 have sizes on the same order of magnitude as the

WO 96/38722

PCT/US96/07555

size of source 110, but each aperture 133 in spatial filter 130 is larger than the corresponding aperture 123 in spatial filter 120.

Spatial filters 120 and 130 provide an array of pixel-beams 115 that are collimated in the sense that each pixel-beam has a minimal semi-shadow component 290 as shown in Fig. 2. Spatial filter 130 removes semi-shadow portion 290 of the radiation passing through filter 120 and removes portion 280 of radiation scattered or Fresnel diffracted by the edges of apertures in spatial filter 120. Spatial filter 130 is removed in some embodiments to increase the intensity of radiation in pixel beams 115 at the expense of increased angular spread and reduced spatial uniformity. Alternatively, one or more additional spatial filters containing progressively larger apertures can be placed between spatial filter 130 and object 140 to better remove radiation scattered at edges of apertures in preceding filters. Typically, the apertures in a spatial filter are circular with a diameter equal to the diameter of the pixel-beam at the plane of the filter, but any shape may be employed. For example, square apertures may increase the efficiency of the detector by increasing the amount of radiation from source 110 used for imaging.

In an exemplary embodiment where source 110 generates X-rays from the K $\alpha$  line of molybdenum, at a wavelength of about 0.71 Å, spatial filter 120 contains a plurality of circular apertures with diameter about 10 to 2000 microns. In security applications such as luggage scanning, relatively large apertures (and pixel-beams) up to about 2 mm in diameter can be used. In medical applications where much higher resolution is desired, typical aperture diameters are from 10 to 50 microns. The aperture size is selected according to Fresnel diffraction effects and the desired resolution

WO 96/38722

PCT/US96/07555

of apparatus 100. The material selected for spatial filters 120 and 130 should have high absorption at given wavelength. For example, copper or tin may be used to absorb X-rays with wavelength of 0.71 Å.

5 Spatial filters 120 and 130 can be formed using conventional technologies for etching and/or laser drilling. Similar techniques with similar accuracy have been used in the manufacture of color CRTs for computer monitors.

10 Pixel-beams 115 diverge from each other. Divergence of pixel beams 115 from each other is useful because the spacing between the centers of the pixel beams increases with distance from source 110 and provides more space for detecting changes in the pixel  
15 beams caused by object 140. The additional space is useful in embodiments which analyze diffraction patterns for each pixel-beam. Additionally, central portions of pixel beams 115 pass unobstructed from source 110 to object 140, increasing the usable energy  
20 from source 110 when compared to systems which require pixel beams to be nearly parallel to each other. Source 110 can be placed closer to spatial filter 120 to provide greater divergence and a more compact measuring system. Using divergent beams utilizes a  
25 larger fraction of the output energy from source 110. For example, beams with a 45° divergence enable the use of up to about 8% of the total flux from source 110. In some systems which rely on refraction, the beams are nearly parallel and typically contain less than  $10^{-4}$  of  
30 the radiation from a source.

A further efficiency provided by detecting diffracted radiation is that more divergence is permitted in each individual beam. Divergence in a beam tends to blur an image but is acceptable when the  
35 divergence is less than the angles being detected. Diffraction angles are relatively large when compared

WO 96/38722

PCI/US96/07553

to the refraction angles used by some other system. Because diffraction angles are relatively large, some embodiments of the invention use divergent pixel-beams, and tolerate small distance between source 110 and spatial filter 120. The distance between source 110 and spatial filter 120 can be one the order of centimeters and provide each pixel beam with a divergence greater than typical angles of refraction.

The separations of centers of apertures 123 in spatial filter 120 are selected according to whether an image is formed and/or diffraction patterns are analyzed. For analysis of diffraction patterns, apertures 123 should be separated from each other by a distance which allows measurement of separate diffraction patterns for each pixel-beam 115. The optimal distance between centers of neighboring apertures 123 depends on the divergence of pixel-beams 115 from each other, the divergence within each pixel-beam 115, the expected angle of diffraction caused by object 140, the distance from source 110 to a detector 170, and the spatial sensitivity of detector 170. The distance between centers of apertures 123 should be such that the diffraction patterns around two adjacent pixel-beams 115 do not overlap at detector 170. However, some overlap is acceptable because mathematical analysis of the intensity patterns can separate radiation diffracted from different pixel-beams 115.

For some types of imaging of object 140, the amount of diffracted radiation is represented in the image, and diffracted radiation from a pixel-beam can overlap with diffracted radiation from a neighboring pixel-beam to increase optical density in the image. Allowing an overlap increases: the number of pixel-beams 115 passing through object 140; the fraction of radiation from source 110 used for imaging in apparatus

WO 96/38722

PCT/US96/07555

100; and the portion of object 140 probed by a single exposure.

Pixel-beams 115 pass through and interact with the matter of object 140. In the course of the interaction radiation of each pixel-beam 115 is partly absorbed, partly refracted, partly non-coherently scattered, and partly diffracted by ordered structures of object 140. Absorption modulates the intensity of a resulting image as in conventional imaging technology. A spatial filter 150 blocks the refracted portion of the pixel-beam and portion which did not interact with matter in object 140.

Spatial filter 150 is between object 140 and detector 170 and contains opaque regions 158 which are attached to intersections in a mesh (not shown). Alternatively, opaque regions 158 could be attached to a transparent material which does not scatter, diffract, or absorb the radiation from source 110. Opaque regions 158 are positioned where pixel-beams 115 would cross the plane of spatial filter 150 if object 140 was absent, and the sizes of regions 158 are selected to block radiation in non-deflected radiation and radiation refracted in object 140. Regions 158 have a shape (circular, square, or other) corresponding to the shape of apertures 123 and 133 in spatial filters 120 and 130.

One embodiment of spatial filter 150 contains regions 158 that are circular caps having the form of cake pans, built from highly absorbing material. The bottom of each caps has radius R, which is

$$R = B + r + d,$$

where B is radius of pixel-beam 115 at the plane of spatial filter 150, r is the broadening of pixel-beam 115 caused by refraction in object 140, and d is the additional broadening which may be caused by diffraction at the edges of apertures 133. In one

WO 96/38722

PCT/US96/07555

implementation, value  $r$  is the displacement caused by about a 10 arc second angle and cuts off all refracted radiation. The walls of the caps are formed from the same material as the bottom and have a height several  
5 times the radius  $R$  of the bottom,  $4 \cdot R$  in some embodiments. The walls of the caps prevent radiation scattered from the cap's bottom from irradiating object 140 or detector 170.

Spatial filter 150 also includes optional opaque  
10 regions 159 which surround opaque regions 158 and block radiation diffracted at large angles. Radiation reaching detector 170 passes through annular openings 153 in spatial filter 150 between opaque regions 158 and 159. A spatial filter 160 placed after spatial  
15 filter 150 and before detector 170 also has opaque regions 168 and 169 which are separated by annular openings 163. Opaque regions 168 correspond to opaque regions 158, and opaque regions 169 correspond to  
20 opaque regions 159. The combination of opaque regions 158, 159, 168, and 169 filter out diffracted radiation which is diffracted at angles outside a range of particular interest for structural analysis. By  
25 selecting the sizes of opaque regions 158, 159, 168, and 169, a specific range of angles of diffracted radiation can be detected. The resulting diffraction pattern which is available for measurement at detector 170 could, for example, be a set of diffraction reflexes which identify particular types of structures or chemicals with object 140.

30 The angles of radiation detected by detector 170 can be varied by changing spatial filters 150 and 160. In one embodiment of the invention, regions 158 have adjustable size and can be expanded to filter radiation which is diffracted at angles less than some particular  
35 angle of the specific interest for structural investigation. In another embodiment of the invention,

WO 96/38722

PCT/US96/07555

spatial filters 150 and 160 are movably mounted so that the distances between spatial filter 150 and spatial filter 160, and from object 150 to spatial filter 150 or 160 can be varied.

5 For imaging, the brightness of a pixel in an image is proportional to the intensity of radiation diffracted from a corresponding pixel-beam. Spatial filter 160 and regions 159 can be removed to allow all diffracted radiation to pass to detector 170 so that  
10 all of the diffracted radiation is harvested and a brighter image results. Since the intensity of diffracted radiation decreases with increasing angle, large angle diffracted components can be effectively removed from an image formed on film, by controlling  
15 exposure time so that the large angle components do not significantly expose the film.

Detector 170 is a conventional detector such as a photo-film, a luminescent screen and optical system for measuring or recording light resulting when penetrating  
20 radiation strikes the luminescent screen, or a pixellated two-dimensional detector adapted for the type of radiation from source 110. For structural analysis of object 140, digital detectors facilitate numerical processing of measurements of the diffraction  
25 pattern. Typically, a general purpose computer (not shown) such as a personal computer or special purpose analyzer may be connected to detector 170 to perform the required analysis.

Russian patent application No. 94042608/25  
30 (042777), entitled "Method of Obtaining an Object Projection by Means of Penetrating Radiation and an Apparatus for its Implementation", filed November 30, 1994, by Alexey V. Kurbatov and Pavel I. Lazarev, describes detector systems for dark field imaging and  
35 analysis of penetrating radiation and is incorporated by reference herein in its entirety. The detectors



WO 96/38722

PCT/US96/07555

described in Russian application No. 94042608/25 (042777) can be employed of the present invention.

In an exemplary embodiment of apparatus 100, source 110 is an X-ray source which emits radiation having wavelength of 0.3 Å from a focal area having a radius of 10 microns. Spatial filter 120 is 0.2 m from source 110 and has circular apertures 123 with radius of 10 microns and center-to-center distance of 45 microns. Spatial filter 120 is made of a material such as lead (Pb) or zirconium (Zr) which is good absorber of 0.3 Å X-rays. The material of a spatial filter is desired to be a good absorber of the radiation with relatively little scattering at the wavelength of the radiation used. The X-rays absorption and scattering properties of many materials are listed in commonly used handbooks dealing X-ray physics and structural analysis. See, for example, "The Powder Methods in X-ray Crystallography" by L.V. Azaroff and M.J. Buerger, 1958, London, Toronto. The thickness of spatial filter 120 depends on the material used, and for the case of lead is about 750 microns.

In the exemplary embodiment, spatial filter 130 is absent, and spatial filter 150 is 0.09 m from spatial filter 120. Object 140 has a thickness of about 0.06 m and a front edge that is next to spatial filter 120, making the back edge of object 140 0.03 m from spatial filter 150. With this geometry, undeflected pixel-beams have a radius of 19 microns and a center-to-center distance of about 65 microns at the plane of detector 170. Opaque regions 158 in spatial filter 150 have radius of 21 microns which is slightly larger the radius of the initial beam at the plane of spatial filter 120. Regions 159 are absent, and gaps between regions 158 which are about 23 microns wide allow diffracted radiation to pass through spatial filter 150 to detector 170. In the exemplary embodiment, opaque

WO 96/38722

PCI/US96/07555

regions 158 are caps having walls extending toward object 140. The walls stop radiation at large angles, which could otherwise pass through spatial filter 150. The walls on a region 158 reduce the angle of radiation which can pass through an adjacent gap in spatial filter 150. Accordingly, adding walls to opaque regions 158 makes spatial filter 150 more angle sensitive. Spatial filter 160 can be added to further increases angle sensitivity. By choosing distances and sizes of components in filters 150 and 160, one can create filter systems of different angle sensitivity.

Table 1 indicates diffraction angles and reflex radii, at spatial filter 150 in the exemplary embodiment, for reflexes of typical biological materials. Material at the front edge of object 140 (left edge in Fig. 1) produces larger reflexes than material at the back edge of object 140 because the back edge is closer to spatial filter 150.

Table 1.

Periodicity D (material)	Diffraction Angle $2\theta$	Radius of reflex from front edge diffraction	Radius of reflex from back edge diffraction
48 Å (mucus)	0.36°	560 µm	180 µm
143 Å (muscle)	0.12°	180 µm	60 µm
200 Å (cartilage)	0.08°	126 µm	40 µm
429 Å (muscle)	0.04°	63 µm	20 µm

In some embodiments, spatial filters 150 and 160 remove reflexes having large radii that spread radiation across multiple pixels. This improves image resolution because radiation from each pixel beams is confined to a smaller area in the image. For example, spatial filters 150 and 160 can remove the radiation that forms the reflex from mucus corresponding to

WO 96/38722

PCT/US96/07555

periodicity of 48 Å. This reflex has a large angle of diffraction ( $0.36^\circ$ ) which creates at spatial filter 150 a large reflex (560 microns) when diffraction takes place at the front edge of object 140. About ten  
5 different gaps between regions 158 receive radiation from this reflex of mucus which blurs the image across ten pixels. Accordingly, the resolution of a projection is lower using the reflex corresponding to 48 Å periodicity in mucus than the resolution using a  
10 reflex corresponding to a longer periodicity. For example, a reflex for mucus corresponding to periodicity 90 Å, which is not listed in the table above, is about as bright as the reflex for periodicity of 48 Å and has a reflex radius of about 390 microns.  
15 This provides almost twice the resolution as the 48 Å reflex.

Placing object 140 closer to spatial filter 150 also enhances resolution. Resolution (or the size of the reflex from diffraction at the front edge of object  
20 140) improves by a factor 1.3 if the back edge of object is 0.01 m from filter 150 instead of 0.03 m. Reflexes from the back edge of object 140 are 3 times smaller. Smaller wavelengths create better resolution because all reflexes are diffracted at smaller angles  
25 and resolve details with better accuracy. Tomography or analysis of multiple projections of object 140 from different angles can also improve resolution of the diffracting tissue.

The embodiment of Fig. 1 contains spatial filters  
30 120, 130, 150, and 160 and detector 170, all of which are planar. Alternatively, spatial filters 120, 130, 150, and 160 and detector 170 can be spherical in form which corresponds to the form of the radiation front emitted by source 110. In this case, spatial filters  
35 120, 130, and 160 are portion of spheres of absorptive material, centered on source 110, and containing

WO 96/38722

PCT/US96/07555

regularly spaced apertures. For spherical spatial filters, apertures having the same size transmit equal amounts of radiation. For planar filters, the angle of incidence and intensity of radiation changes with distance from source 110. To provide uniform intensity pixel-beams 115 in some embodiments, the size and shape of apertures 123, 133, 153, and 163 vary across the surface of the spatial filters 120, 130, 150, and 160.

In a second exemplary embodiment, source 110 is at the center of semi-spherical spatial filter 120, and the distance between source 110 and spatial filter 120 is such that apertures 123 create pixel-beams 115 that diverge from each other and have a center-to-center separation at spatial filter 150 that is larger than the radius of the reflexes produced by object 140. With this geometry, the diffraction patterns can be used for imaging of object 140 and/or for detailed analysis of the angular and axial distributions of intensity in a diffraction pattern from each pixel-beam 115.

In addition to structural analysis and forming images of object 140 using a single projection of pixel-beams 115 through object 140, object 140 can be rotated to form multiple projections. Well known tomography techniques can be employed to provide three-dimensional maps of the structure of object 140.

Figs. 3 and 4 show alternative embodiments of spatial filters between object 140 and detector 170. A pixel-beam has a portion I+R which either did not interact with object 140 or was refracted by object 140. Portion I+R is blocked by region 158. The non-coherently scattered portion of radiation is typically deflected at angles larger than the diffraction angles, and is absorbed by a spatial filter 360 (Fig. 3) or a spatial filter 460 (Fig. 4).

WO 96/38722

PCT/US96/07555

The embodiment of Fig. 3 differs from the embodiment of Fig. 4 in that spatial filter 360 contains opaque regions 368 in central portions of each aperture 363 and in that apertures 363 in spatial filter 360 are larger than apertures 463 in spatial filter 460. By changing form and size of opaque regions 368 and/or apertures 363, a desired angular range of diffracted light can be selected for detection by detector 170 to obtain images or analysis of particular diffraction angles.

Figs. 3 and 4 show diffracted radiation for two types of structures inside object 140, one structure X diffracts radiation at an angle  $\alpha$  and another structure Y diffracts radiation at an angle  $\beta$ . Spatial filter 360 blocks radiation at angle  $\alpha$  for imaging object 140 using radiation diffracted at angle  $\beta$ . Spatial filter 460 blocks radiation at angle  $\beta$  for imaging of object 140 using radiation diffracted at angle  $\alpha$ . Imaging object 140 twice, once with spatial filter 360 and once with spatial filter 460, shows the presence and locations of structures X and Y. The two step process eliminates overlapping of radiation which could obscure the location of structure X or Y.

A non-invasive imaging process using apparatus 100 for detecting the presence of an abnormal tissue such as cancer in a patient can be implemented using measurable differences in the diffraction patterns for normal and abnormal tissue. For example, normal and sickle anemic erythrocytes have distinct diffusive scattering patterns. Similarly, mucus from normal and from sub-lethal irradiated rats have different distinct diffraction patterns. To identify and locate abnormal tissue, a patient can be imaged using a spatial filter 360 that selects radiation diffracted at an angle  $\beta$  known to be present in the diffraction pattern for the abnormal tissue. Spatial filter 360 is replaced with

WO 96/38722

PCT/US96/07555

spatial filter 460 to select radiation diffracted at angle  $\alpha$  present in the diffraction pattern of normal tissue, and the patient is imaged again. The two images can be compared to determine the presence and location of abnormal tissue relative to normal tissue.

- 5        Although the present invention has been described with reference to particular embodiments, the description is only an example of the invention's application and should not be taken as a limitation.
- 10      In particular, even though much of preceding discussion was aimed at forming images using X-ray radiation, alternative embodiments of the invention include use of other penetrating radiations such as neutrons which have wavelengths similar to X-rays. Various other
- 15      adaptations and combinations of features of the embodiments disclosed are within the scope of the present invention as defined by the following claims.

WO 96/38722

PCT/US96/07555

We claim:

1. A method for examining the structure of an object, comprising:
  - irradiating the object with a plurality of
  - 5 pixel-beams which diverge from each other; and
  - detecting, for each of the pixel-beams, an intensity of diffracted radiation around a non-deflected path of each of the pixel-beam.
- 10 2. The method of claim 1, wherein detecting intensity for a pixel-beam comprises measuring an integral of the intensity of the diffracted radiation around the pixel-beam.
- 15 3. The method of claim 1, wherein detecting intensity for a pixel-beam comprises measuring a diffraction pattern around the pixel-beam.
- 20 4. The method of claim 3, wherein measuring the diffraction pattern comprises measuring an angle at which the diffraction pattern has a reflex.
- 25 5. The method of claim 1, wherein detecting intensity for a pixel-beam comprises:
  - blocking radiation which is outside a range of angles with the pixel-beam; and
  - measuring intensity of radiation within the range of angles.
- 30 6. The method of claim 1, further comprising irradiating a first spatial filter with a penetrating radiation, wherein the first spatial filter has a first array of apertures formed therethrough and radiation which passes through the first array of apertures forms
- 35 the pixel-beams.

WO 96/38722

PCT/US96/07555

7. The method of claim 6, further comprising irradiating a second spatial filter with the penetrating radiation which passes through the first array of apertures, wherein the second spatial filter  
5 has a second array of apertures formed therethrough, wherein each aperture in the second array is centered along a line which passes through the source and a center of a corresponding aperture in the first array.

10 8. The method of claim 1, wherein irradiating the object comprises irradiating the object with pixel-beams that are sufficiently separated that diffraction patterns caused by diffraction of neighboring pixel-beams in the object do not overlap where diffracted  
15 intensity is detected.

9. The method of claim 1, further comprising filtering radiation which passes through the object to remove radiation not deflected by the object and  
20 radiation refracted in the object, wherein filtering occurs before detecting intensity.

10. A diagnostic procedure comprising:  
irradiating a tissue with a first plurality  
25 of pixel-beams of a penetrating radiation, wherein the pixel-beams simultaneously pass through the tissue; and  
measuring, for each pixel-beam, radiation  
which exits the tissue at a first angle relative  
30 to a non-deflected path of that pixel-beam,  
wherein the first angle corresponds to a reflex found in a diffraction pattern for an abnormal tissue.



WO 96/39722

PCT/US96/07555

11. The procedure of claim 10, further comprising spatially filtering radiation which exits from the tissue surrounding a non-deflected path of a pixel beam, wherein the filtering selects radiation within a first range of angles with the non-deflected path, and the first range includes the first angle.

12. The procedure of claim 10, wherein the pixel-beams are divergent from each other.

13. The procedure of claim 10, wherein measuring comprises forming an image of the tissue, wherein the image comprises pixels that correspond to the pixel-beams, each pixel having an intensity which depends on an intensity of radiation diffracted from a corresponding pixel beam, at the first angle with the corresponding pixel beam.

14. The method of claim 10, further comprising:  
irradiating a tissue with a second plurality of pixel-beams of the penetrating radiation, wherein the second plurality of pixel-beams simultaneously pass through the tissue;  
measuring, for each pixel-beam in the second plurality, radiation which exits the tissue at a second angle relative to a non-deflected path of that pixel-beam, wherein the second angle corresponds to a reflex found in a diffraction pattern for a normal tissue; and  
comparing the measurement of the radiation at the first angle to the measurement of the radiation at the second angle.

WO 96/38722

PCT/US96/07555

15. An apparatus for examining an object,  
comprising:

a source of penetrating radiation;

5 a first spatial filter positioned to divide  
radiation from the source into a plurality of  
separate beams which simultaneously irradiate the  
object;

10 a second spatial filter positioned to filter  
radiation from the beams which emerges from the  
object, the second spatial filter having an array  
of separate regions which are opaque to the  
penetrating radiation, wherein each opaque region  
corresponds to one of the beams and is positioned  
and sized to block radiation from the  
15 corresponding beam which passes undeflected  
through the object and block radiation from the  
corresponding beam which is refracted by the  
object; and

20 a detector of the penetrating radiation  
positioned to measure radiation from the beams,  
which passes through the second filter.

16. The apparatus of claim 15, wherein the first  
spatial filter comprises a layer of material which is  
25 opaque to the penetrating radiation, the layer having  
an array of apertures formed therethrough.

17. The apparatus of claim 16, further comprising  
a third spatial filter which comprises an opaque layer  
30 having an array of apertures formed therethrough,  
wherein each aperture through the third spatial filter  
is along a line through the source and a corresponding  
one of the apertures in the first spatial filter and is  
larger than the corresponding aperture in the first  
35 spatial filter.

WO 96/38722

PCI/US96/07555

18. The apparatus of claim 16, wherein the layer of material is formed in the shape of a portion of a sphere centered on the source.

5 19. The apparatus of claim 15, wherein each opaque region of second spatial filter comprises:  
a bottom region having a normal parallel to  
an undeflected direction of the corresponding  
beam; and  
10 a wall which surrounds a perimeter of the bottom region.

20. The apparatus of claim 15, wherein the opaque regions have a size which can be adjusted by a user.  
15

21. The apparatus of claim 15, wherein the second spatial filter further comprises a layer of material which is opaque to the penetrating radiation, wherein the layer has an array of apertures formed  
20 therethrough, and each of the opaque regions is located in a central portion of one of the apertures through the layer and is surrounded by an area which is transparent to the penetrating radiation.

22. The apparatus of claim 21, wherein the layer of material is formed in the shape of a portion of a sphere centered on the source.  
25

23. A method for examining the structure of an  
30 object, comprising:  
irradiating the object with a spatially modulated radiation pattern, the radiation pattern having dark portions which are void of radiation;  
and  
35 detecting, in each dark portion, an intensity of diffracted radiation.

WO 96/38722

PCT/US96/07555

24. The method of claim 23, wherein:  
the spatially modulated radiation pattern  
comprises a plurality of beams of radiation; and  
the dark portions surround the beams.

WO 96/38722

PCT/US96/07555

## AMENDED CLAIMS

[received by the International Bureau on 6 August 1996 (06.08.96);  
original claims 10,23 and 24 cancelled; original claims 1-3,  
5,6,8,11-14 amended; new claim 25 added; remaining claims  
unchanged (5 pages)]

1. A method for examining the structure of an  
5 object, comprising:  
irradiating the object with a plurality of  
beams which diverge from each other, wherein the  
beams are separated from each other and  
simultaneously pass through the object; and  
10 detecting, for each of the beams, an  
intensity of diffracted radiation around a non-  
deflected path of the beam.
2. The method of claim 1, wherein detecting  
15 intensity for a beam comprises measuring an integral of  
the intensity of the diffracted radiation around the  
non-deflected path of the beam.
3. The method of claim 1, wherein detecting  
20 intensity for a beam comprises measuring a diffraction  
pattern around the non-deflected path of the beam.
4. The method of claim 3, wherein measuring the  
diffraction pattern comprises measuring an angle at  
25 which the diffraction pattern has a reflex.
5. The method of claim 1, wherein detecting  
intensity for a beam comprises:  
blocking radiation which is outside a range  
30 of angles with the beam; and  
measuring intensity of radiation within the  
range of angles.
6. The method of claim 1, further comprising  
35 irradiating a first spatial filter with a penetrating  
radiation, wherein the first spatial filter has a first  
array of apertures formed therethrough and radiation  
which passes through the first array of apertures forms  
the beams.

WO 96/38722

PCT/US96/07555

7. The method of claim 6, further comprising irradiating a second spatial filter with the penetrating radiation which passes through the first array of apertures, wherein the second spatial filter  
5 has a second array of apertures formed therethrough, wherein each aperture in the second array is centered along a line which passes through the source and a center of a corresponding aperture in the first array.

10 8. The method of claim 1, wherein irradiating the object comprises irradiating the object with beams that are sufficiently separated that diffraction patterns caused by diffraction of neighboring beams in the object do not overlap where diffracted intensity is  
15 detected.

9. The method of claim 1, further comprising filtering radiation which passes through the object to remove radiation not deflected by the object and  
20 radiation refracted in the object, wherein filtering occurs before detecting intensity.

Claim 10 is canceled.

25 11. A diagnostic procedure comprising:  
irradiating a tissue with a first plurality of beams of a penetrating radiation, wherein the beams are separated from each other and simultaneously pass through the tissue;  
30 spatially filtering radiation which exits from the tissue, wherein for each beam, the filtering selects radiation within a first range of angles with a non-deflected path of the beam, and the first range includes a first angle that  
35 corresponds to a reflex found in a diffraction pattern for an abnormal tissue; and

WO 96/38722

PCT/US96/07553

measuring, for each beam, radiation which exits the tissue at the first angle relative to the non-deflected path of that beam.

5 12. The procedure of claim 11, wherein the beams are divergent from each other.

10 13. The procedure of claim 11, wherein measuring comprises forming an image of the tissue, wherein the image comprises pixels that correspond to the beams, each pixel having an intensity which depends on an intensity of radiation diffracted from a corresponding beam, at the first angle with the corresponding beam.

15 14. The method of claim 11, further comprising: irradiating a tissue with a second plurality of beams of the penetrating radiation, wherein the second plurality of beams simultaneously pass through the tissue;

20 measuring, for each beam in the second plurality, radiation which exits the tissue at a second angle relative to a non-deflected path of that beam, wherein the second angle corresponds to a reflex found in a diffraction pattern for a normal tissue; and

25 comparing the measurement of the radiation at the first angle to the measurement of the radiation at the second angle.

30 15. An apparatus for examining an object, comprising:

a source of penetrating radiation;  
a first spatial filter positioned to divide radiation from the source into a plurality of  
35 separate beams which simultaneously irradiate the object;

WO 96/38722

PCT/US96/07555

5 a second spatial filter positioned to filter radiation from the beams which emerges from the object, the second spatial filter having an array of separate regions which are opaque to the penetrating radiation, wherein each opaque region corresponds to one of the beams and is positioned and sized to block radiation from the corresponding beam which passes undeflected through the object and block radiation from the corresponding beam which is refracted by the object; and

10 a detector of the penetrating radiation positioned to measured radiation from the beams, which passes through the second filter.

15

16. The apparatus of claim 15, wherein the first spatial filter comprises a layer of material which is opaque to the penetrating radiation, the layer having an array of apertures formed therethrough.

20

17. The apparatus of claim 16, further comprising a third spatial filter which comprises an opaque layer having an array of apertures formed therethrough, wherein each aperture through the third spatial filter is along a line through the source and a corresponding one of the apertures in the first spatial filter and is larger than the corresponding aperture in the first spatial filter.

25

18. The apparatus of claim 16, wherein the layer of material is formed in the shape of a portion of a sphere centered on the source.

30

19. The apparatus of claim 15, wherein each opaque region of second spatial filter comprises:

35



WO 96/38722

PCT/US96/07555

a bottom region having a normal parallel to  
an undeflected direction of the corresponding  
beam; and

5 a wall which surrounds a perimeter of the  
bottom region.

20. The apparatus of claim 15, wherein the opaque  
regions have a size which can be adjusted by a user.

10 21. The apparatus of claim 15, wherein the second  
spatial filter further comprises a layer of material  
which is opaque to the penetrating radiation, wherein  
the layer has an array of apertures formed  
therethrough, and each of the opaque regions is located  
15 in a central portion of one of the apertures through  
the layer and is surrounded by an area which is  
transparent to the penetrating radiation.

20 22. The apparatus of claim 21, wherein the layer  
of material is formed in the shape of a portion of a  
sphere centered on the source.

Claim 23 is canceled.

25 Claim 24 is canceled.

25. The method of claim 1, further comprising  
filtering radiation which exits from the object to  
remove radiation not deflected by the object, wherein  
30 filtering occurs before detecting intensity.

WO 96/38722

PCI/US96/07555

STATEMENT UNDER ARTICLE 19

The above amendments and addition to the claims are believed fully supported by the specification and drawings in the international application as filed. Fig. 1, for example, shows pixel beams separated from each other and

WO 96/38722

PCT/US96/07555

1/4

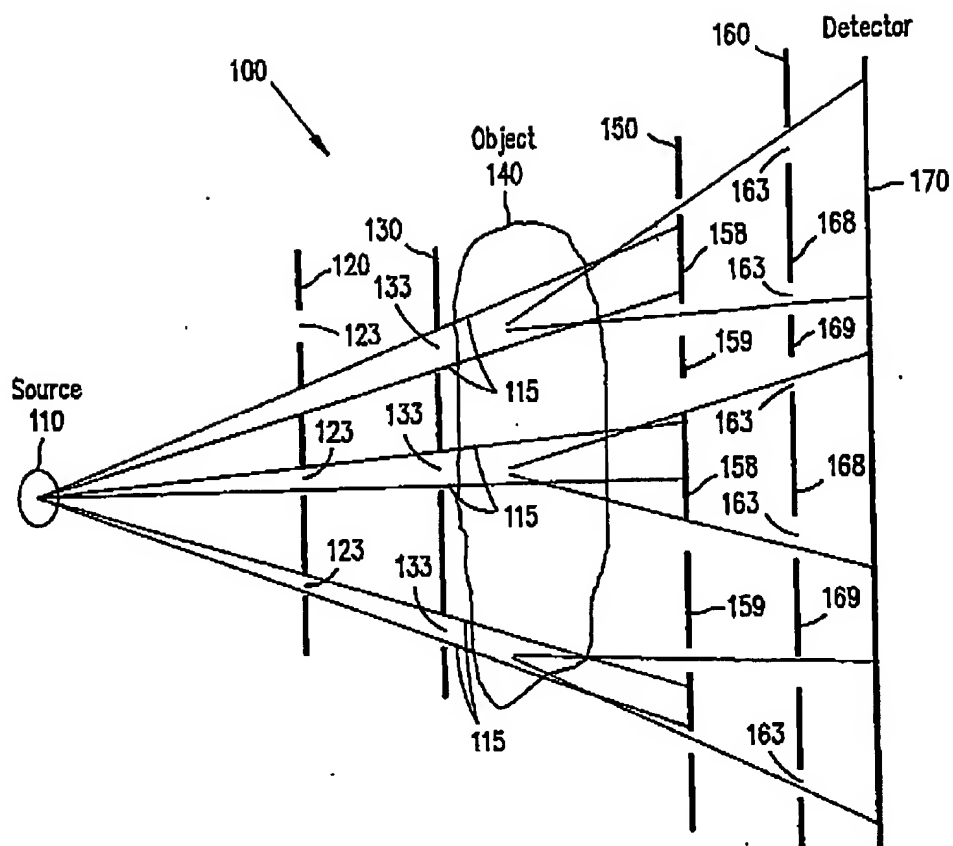


FIG. 1

WO 96/38722

PCT/US96/07555

2/4

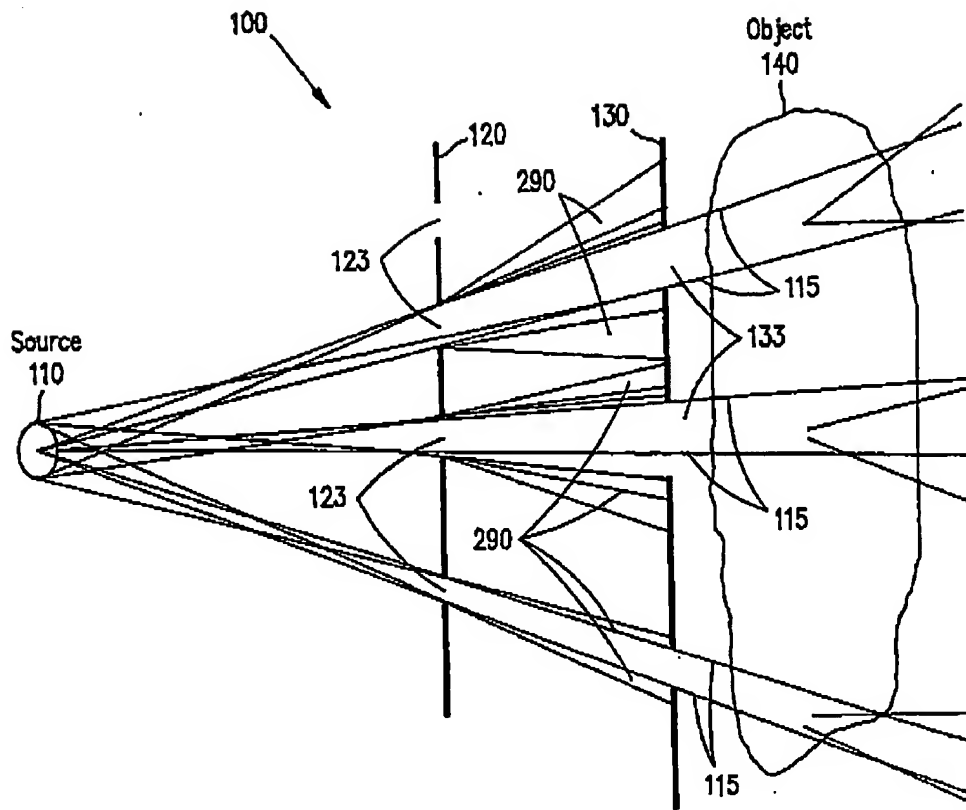


FIG. 2

WO 96/38722

PCT/US96/07555

3/4

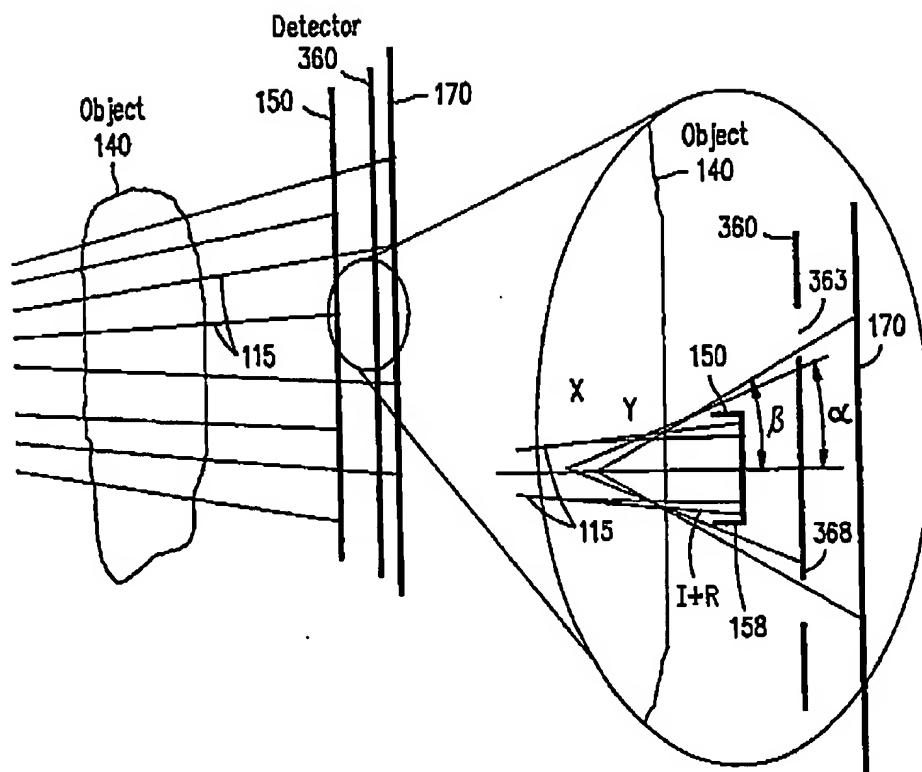


FIG. 3

WO 96/38722

PCT/US96/07555

4/4

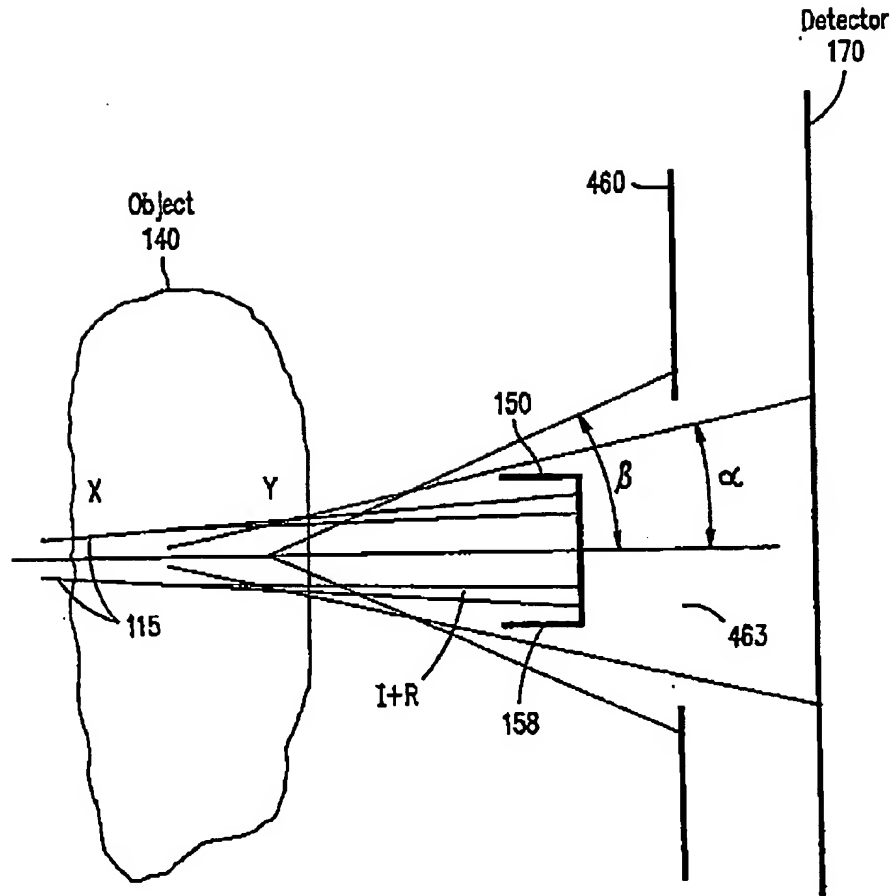


FIG. 4

## INTERNATIONAL SEARCH REPORT

 International application No.  
 PCT/US96/07555

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : G01N 23/20

US CL : 378/71

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 378/71

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,P Y	US, A, 5,491,738 (Blake et al) 13 February 1996 See the entire document.	23 1-6,8,10,12-14,24

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reasons (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later documents published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" documents of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"Z" document member of the same patent family

Date of the actual completion of the international search

02 JULY 1996

Date of mailing of the international search report

08 JUL 1996

 Name and mailing address of the ISA/US  
 Commissioner of Patents and Trademarks  
 Box PCT  
 Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

 Craig Church  
 Telephone No. (703) 305-4861

Form PCT/ISA/210 (second sheet) (July 1992)\*